

A said 7 to 25 contiguous amino acids at least 3 contiguous amino acid residues of SEQ ID NO:19 or SEQ ID NO:20 or SEQ ID NO:21 or SEQ ID NO:22 or SEQ ID NO:23 or SEQ ID NO:24.

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#### **REMARKS**

Claims 1-4, 7-12, 18-20, 30, 34-36, 41, 55-57, 62 and 70 were examined. In response, Applicant has amended Claim 4. Favorable reconsideration and allowance of the application is respectfully requested.

#### **Rejection Under 35 U.S.C. § 112, second paragraph**

Claims 1, 12, 18, 30, 34, 35, 41, 55, 56 and 62 have been rejected as indefinite in the use of wth3 as the only means of identifying the claimed polypeptides. Applicants respectfully direct the attention of the Examiner to the specification where structural characterizations can be found. Structural information concerning the identity of the gene is found, for example, at page 28, lines 15-16. The map position for WTH3 is 2q31 on the long arm of chromosome 2, adjacent to a Sequence Tagged Site (STS) identified as CHLC.GATA27A12. The specification also discloses a corresponding mRNA of 3 kb, the level which is about 10 times greater in MCF7 cells than in MCF7/Adr cells (page 29, ll. 18-21). Furthermore, the nucleotide sequence encoding wth3 and the amino acid sequence of the encoded protein have extensive regions of homology and distinct differences as compared to rab6 and the nucleotide sequence encoding rab6 as depicted in Figs. 1 and 2.

Applicant submits that, based on these and other disclosures in the specification, one of skill in the art could easily ascertain the claimed molecules based on the disclosed structural characteristics. Accordingly, Applicant requests that the rejection for indefiniteness for recitation of "wth3" be withdrawn.

#### **Rejection Under 35 U.S.C. § 112, first paragraph**

Claims 4, 7-12, 18, 19, 30, 34-36, 41, 55-57 and 62 have been rejected under 35 U.S.C. § 112, first paragraph, because the specification is not enabling for the scope of the claims.

Claim 4 is amended to more clearly recite that the claimed immunogenic fragments of wth3 include within the claimed 7-25 contiguous amino acids of SEQ ID NO:12, at least three contiguous amino acids from one of SEQ ID NOS:19, 20, 21, 22, 23 or 24. That is, the claimed immunogenic fragments include epitopes which distinguish wth3 from rab6.

The Examiner asserts that the specification does not enable immunogenic fragments derived from SEQ ID NO:12 as recited in Claims 4 and 7-12. The Examiner has cited Paul, Klein and Chen for principles such as self-tolerance, repertoire of antigenic sites, and factors determining binding of an antigenic determinant to an antibody. Applicants respectfully disagree with the Examiner's position.

According to the specification, immunogenic fragments of the specification comprise amino acids of SEQ ID NOS: 19, 20, 21, 22, 23 or 24. (Specification, page 3, ll. 18-21). That is, immunogenic fragments of the invention are those portions of wth3 that can be used to generate wth3 specific antibodies. Thus, all claimed fragments comprise contiguous amino acids of wth3 (SEQ ID NO:12), and within those contiguous amino acids include contiguous amino acids that differentiate wth3 from rab6. The specification identifies the amino acids unique to wth3 (see, e.g., Fig. 2). The specification further discloses properties of peptides useful for obtaining antigen-specific antibodies (page 21, ll. 4-13), methods for identifying desired epitopes (page 21, ll. 14-19), and methods for identifying monoclonal and polyclonal antibodies which bind to distinguishing epitopes of otherwise similar antigens (page 21, ll. 20-29). Further, the range of useful epitopes is not limited by antigenicity in a host organism. The specification discloses that antibodies can be obtained using protein fusions or by displaying epitopes on the surface of filamentous phage (e.g., page 21, lines 22-24). Thus, responses to epitopes of interest can be generated even where the epitope is not immunogenic in its native context.

Applicants believe that the specification is fully enabling for the immunogenic fragments of Claims 4 and 7-12 and respectfully request that the rejection be withdrawn.

Claims 18, 19, 30, 34-36, 41, 55-57 and 62 have been rejected as drawn to non-disclosed nucleic acids that are not enabled by the specification. Claims 18 and 19 are drawn to sequences of adjacent nucleotides of SEQ ID NO:10 that hybridize to WTH3 but not to RAB6.

Claims 30, 34-36, 41, 55-57 and 62 are drawn to nucleic acid probes, oligonucleotides, and kit comprising such, that hybridize with and/or amplify WTH3 and not RAB6 under stringent hybridization conditions. Applicants respectfully traverse this rejection.

The specification discloses stringent hybridization conditions as conditions that allow hybridization of nucleic acids which are greater than 90% homologous, but prevent hybridization of nucleic acids which are less than 70% homologous. It is also disclosed that where there is extensive homology, it may be desirable to further increase stringency. Such adjustment of stringency is well within the capability of one of ordinary skill in the art, and the specification points to guidelines for predicting stringency. (Specification, page 17, ll. 21-30).

One use of nucleotide acids of the invention is to determine expression of WTH3, RAB6C, RAB6, or a homolog (page 18, line 31 to page 19, line 5). A homolog is a protein having about 80% or greater identity, more preferably 90% or greater identity to wth3, rab6c, or rab6 over the sequence which corresponds to rab6. (Not all of wth3 corresponds to rab6 as wth3 has an additional 46 amino acids at the carboxy terminus.)

The specification provides a clear comparison between the coding sequence of WTH3 and the coding sequence of RAB6 (Fig.1). The specification also provides a similar comparison between RAB6C and RAB6 (Fig. 3). Notably, upon inspection of the regions of non-homology as disclosed in Figs. 1 and 3, it would be clear to one of ordinary skill in the art that the sequence of RAB6C is more similar to WTH3 than to RAB6. Furthermore, it would be within the capability of one of ordinary skill in the art to select nucleotide probes or oligonucleotide primers that selectively hybridize to or amplify the desired species.

The specification discloses properties of probes and oligonucleotides that differentially hybridize to WTH3 or RAB6. Example 2 discloses that a WTH3 specific probe identifies a 3 kb transcript by northern analysis (page 29, ll. 12-23). In contrast, a RAB6 probe identifies a series of transcripts ranging from 1.5 kb to over 4 kb (page 8, ll. 28-30; page 30, ll. 4-20). The hybridization conditions are described (page 29, ll. 9-10). Example 2 discloses oligonucleotide primers designed to selectively amplify RAB6 sequences or WTH3/RAB6C

sequences (page 30, l. 21 to page 31, l. 2). Differential amplification of the selected species is disclosed in Fig. 7 (page 8, l. 30 to page 9, l. 8).

Taken together, it is Applicants belief that these portions of the specification clearly enable one of ordinary skill in the art to practice the claimed invention. Accordingly, withdrawal of this ground of rejection is respectfully requested.

**Conclusion**

In view of the foregoing amendment and remarks, it is believed that the present application is in a condition for allowance which action is earnestly solicited.

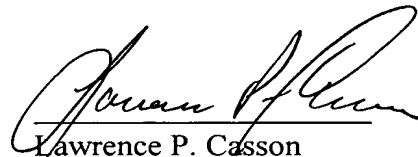
The Examiner is invited, after consideration of the present response, to contact the undersigned to discuss any issue in this case that would expedite allowance of the subject application.

Respectfully Submitted,

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